## REMARKS

Claims 1-27 are all the claims pending in the application, prior to the present amendment.

Applicants have canceled claims 1-27, and have added new claims 28-37.

New claims 28 and 29 correspond to original claim 24, but are rewritten as independent claims. New claims 30 and 31 are based on original claims 3 and 12, respectively. New claims 32-34 correspond to original claims 25-27. In new claim 35, the "humans" are limited to middle-aged or older persons. These amendments are supported by page 8, lines 10-15, of the specification. In new claim 36, the "fatigue" has been limited to physical exhaustion during or after sickness. This amendment is supported by the specification at page 1, last two lines to page 2, line 2. In new claim 37, the "fatigue" has been limited to muscle fatigue. This amendment is supported by, for example, the specification at page 7, line 11 to page 8, line 6, page 13, lines 25-26, Examples 1 and 2, and original claim 12.

Claims 5 and 8 have been rejected under the first paragraph of 35 U.S.C. § 112 as containing subject matter that was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Examiner objects to the term "derivatives."

As discussed above, applicants have canceled claims 1-27 and have added new claims 28-to 37. The new claims do not refer to "derivatives." Accordingly, this rejection is moot.

Claims 1-3 have been rejected under 35 U.S.C. § 102(b) as anticipated by WO 98/07417.

As discussed above, claims 1-3 have been canceled. Claims 1-3 were directed to a product or composition containing a reduced coenzyme Q. The new claims that appear in the present application are not directed to a product or composition, but are directed to a method. Applicants submit that this rejection is moot in view of the cancellation of claim 1-3.

Claims 1-27 have been rejected under 35 U.S.C. § 103(a) as obvious over WO 98/07417 (Mae et al), in view of the following five Japanese references: JP 10-287560; JP 10-53520; JP 7-330584; JP 7-330593; and JP 2002-363073.

As discussed above, applicants have canceled claims 1-27 and have added new claims 28-37, with claims 28 and 29 being independent.

Claim 28 is directed to a method for reducing fatigue in animals in the state of fatigue, which comprises administering, to said animals, a fatigue reducing agent comprising reduced coenzyme Q represented by formula (1) of claim 28 as an active ingredient.

Claim 29 is also directed to a method for reducing fatigue in animals by administering a fatigue reducing agent, and recites that the fatigue reducing agent comprises the reduced coenzyme Q of formula (1) and oxidized coenzyme Q of formula (2).

Applicants submit that the cited documents do not disclose or render obvious the subject matter of claims 28-37 and, accordingly, request withdrawal of this rejection.

WO 98/07417 corresponds to JP 10-109933 that is cited at page 4 of the present application and corresponds to U.S. 6,184,255 to Mae et al (Mae et al '255), which is of record in the present application. In the following discussion, applicants will refer to Mae et al '255 when describing the teachings of WO 98/07417.

Each of the five Japanese documents were cited by applicants in Information Disclosure Statements. In addition, JP 10-287560, JP 7-330584, JP 7-330593 have been cited by applicants at page 3 of the present specification.

WO 98/07417 states that "the demand for coenzyme Q10 is increased in normal subjects in the state of severe physical fatigue and patients with cardiovascular disease, chronic debilitating disease, or on prolonged pharmacotherapy." (Emphasis added.) Column 1, lines 33-36 of Mae et al '255.

JP 10-287560 discloses an anti-fatigue effect of oxidized coenzyme Q10 (known as ubiquinone or ubidecarenone), which was determined by forcing a rat attached with a spindle to swim for 2 hours. This fatigue loading test involved a fatigue reducing effect of oxidized coenzyme Q10 under very severe fatigue-loading conditions where the spontaneous motor activity of the rat after loading decreased to 24.1% of that before loading, despite a long-time observation for 24 hours.

While the cause of fatigue has not been scientifically clarified, one of the certain causes is energy depletion. As disclosed in JP 10-287560, when severe fatigue is observed that limits movement for a long period of 24 hours after physical exercise, the energy depletion is considered to have occurred systemically. To reduce the severe systemic fatigue, it is necessary to distribute nutrition throughout the body. Coenzyme Q having cardiac function activating activity is considered suitable for supplying nutrition to the entire body because it enhances blood flow. Moreover, a fatigue reducing action based on a mitochondria activating activity (increased ATP biosynthesis) of coenzyme Q itself is also expected.

With this background, it is considered that WO 98/07417 presents a potential of coenzyme Q against severe fatigue, and JP 10-287560 discloses the usefulness of oxidized coenzyme Q by the actual use of a severely fatigued model. Usefulness can also be assumed, in view of the disclosure in JP 10-287560, of the action of oxidized coenzyme Q on the cardiac muscle.

JP 7-330584 and JP 7-330593 disclose a fatigue ameliorant characteristically containing ubiquinone and carnitine or ubiquinone and biotin, respectively, as active ingredients. In the Examples, a forced exercise test using a tread mill was performed. The exercise load (overfatigue from running at 100 m/min for 3 minutes, or at 40 m/min for 120 min x 10 days) is greater than the load in the present application. Thus, using a severely fatigued model, JP 7-330584 and JP 7-330593 disclose the usefulness of ubiquinone, and carnitine or biotin.

JP 2002-363073 discloses a sport-performance improving agent characteristically containing ubiquinone as a main active ingredient, and teaches that the agent is effective for fatigue caused by physical exercise. In fact, it discloses a fatigue reducing effect when professional athletes or highly trained athletes kept training for 40 days. Thus, JP 2002-363073 discloses usefulness of ubiquinone using a severely fatigued model.

JP 10-53520 describes an antifatigue agent containing a compound represented by formula (I) of JP 10-53520, such as idebenone, or a hydroquinone form thereof as an active ingredient. However, C5 in the chemical formula of coenzyme Q10 in the present application has a branched-chain structure, whereas C5 of the compound of JP 10-53520 has a non branched-chain structure (-$(CH_2)$n). Thus, the present invention differs from the invention

disclosed in JP 10-53520 since the chemical structures are different. JP 10-53520 provides no information relating to the antifatigue effect of coenzyme Q10.

As described above, the anti-fatigue effect of coenzyme Q as disclosed in the cited references only means that oxidized coenzyme Q10 is useful for severe physical fatigue.

In contrast, mild fatigue is mainly caused by local fatigue of the muscle in use, and is different in that the systemic energy depletion as disclosed in the cited references is void. The present invention relates to, as described in the specification, recovery from and prevention of physical exhaustion caused by exercise, i.e., muscle fatigue, physical exhaustion during and after sickness, and fatigue cased by aging. The present invention is not drawn to severe fatigue. For example, in the tread mill test performed in Examples 3 and 4 of the present specification, rats were forced to run on a belt conveyor, where the level of fatigue can be varied by changing the running speed. Under the conditions adopted in the Examples of the present specification, i.e., running with a speed of 10 m/min with a stepwise increase by 5 m/min every 3 minutes, the rats after running recovered in a relatively short time of about 1 hour and could move almost as usual. Thus, the rats were ordinary fatigue models.

The effectiveness of reduced coenzyme Q10 for such mild fatigue was found for the first time by the present invention.

The cited references do not disclose that reduced coenzyme Q further increases the amount of coenzyme Q in the muscle, namely, that it provides a further effect for muscle fatigue, as compared to conventional oxidized coenzyme Q which has been actually confirmed to have a (severe) fatigue reducing effect.

Further, in Example 4 of the present application, the results of the tread mill test in aged rats show a running time prolongation effect of 7 times or longer by reduced coenzyme Q than that by oxidized coenzyme Q, and this is an unexpected effect. The results cannot be explained solely with the absorbability enhancing effect of reduced coenzyme Q as described in WO 98/07417.

Moreover, the cited references do not describe a striking effect of reduced coenzyme Q in aged animals. In Example 4 of the present application, the 61- to 63-week-old rats used here in the test correspond to humans in the 30's. That is, the cited references neither teach nor suggest that reduced coenzyme Q shows a surprising fatigue reducing effect even in middle-aged and older persons, for whom oxidized coenzyme Q cannot exhibit an effect easily.

Therefore, applicants submit the present invention cannot be arrived at from the cited references, even if the teachings of WO 98/07417 are combined with the teachings of the other cited references. To conclude, applicants submit that the present invention is not obvious from the cited references.

In view of the above, applicants submit that the cited documents do not disclose or render obvious the subject matter of claims 28-37 and, accordingly, request withdrawal of this rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

Sheldon I. Landsman

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Sheldon I. Landsman
Registration No. 25,430

Date: February 7, 2008